## REMARKS

These remarks are in response to the Office Action dated August 13, 2003. Claims 31-42 are withdrawn as drawn to a non-elected invention. Applicants note their intention to rejoin appropriate method claims once the composition claims have been found allowable, in accordance with the rejoinder procedure in MPEP §821.04.

Claims 1-30 have been canceled without prejudice to Applicants' right to prosecute the canceled subject matter in any divisional, continuation, continuation-in-part or other application. Claims 43-63 have been added in the present amendment. Support for the new claims can be found throughout the originally filed specification. Specifically, support for claims 43-46 is found e.g., at page 16, lines 3-7. Support for claim 47 can be found at page 12, lines 22-32. Support for claims 48-50 can be found at page 13, lines 15-32, bridging to page 14, lines 1-12. Support for claims 51-53 can be found at page 7, lines 10-30. Support for claims 54 and 55 can be found at page 12, line 6. Support for claims 56-58 can be found at page 16, lines 30-31, through page 17, lines 1-3. No new matter has been added. Applicants respectfully request reconsideration of the present application.

### I. Rejections under 35 U.S.C. §101

Claims 16 and 17 stand rejected under 35 U.S.C. §101 as allegedly claiming an invention that is not supported by either a specific and substantial utility or a well established utility. In addition, claims 16 and 17 stand rejected under 35 U.S.C. §112, first paragraph, as allegedly not enabled by the specification. These rejections are moot with regard to canceled claims 16 and 17. The new claims are limited to polypeptides that either (a) consist of or comprise SEQ ID NO:2 (claims 51 and 52, respectively), or (b) possess enone reductase activity, clearly satisfying the utility requirements of 35 U.S.C. §101. Accordingly, Applicants request that the rejections be withdrawn.

## II. Rejections under 35 U.S.C. §112, Second Paragraph

Claims 3 and 16 stand rejected under 35 U.S.C. §112, second paragraph, as allegedly indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is moot with regard to canceled claims 3 and 16. Applicants traverse this rejection as it may be applied to the pending claims.

Where the new claims include limitations regarding hybridization conditions, such conditions are specified (see new claim 47). In addition, where the new claims include limitations regarding the source of a polypeptide, the source is specified (see new claims 52 and 53). Finally, the new claims no longer recite the allegedly indefinite term "functionally-equivalent."

## III. Rejections under 35 U.S.C. §112, First Paragraph

***Enablement***

Claims 3 and 16 stand rejected under 35 USC §112, first paragraph, because the specification allegedly fails to enable the claimed invention. This rejection is moot in view of the cancellation of claims 3 and 16. Applicants traverse this rejection as it may be applied to the pending claims.

The issue raised in paragraph 8 on page 4 of the Office Action is addressed in new claim 47, which recites a polypeptide encoded by a nucleic acid comprising the "complement" of a nucleic acid that hybridizes under stringent conditions to a nucleic acid comprising the nucleotide sequence of SEQ ID NO: 1.

The issues raised in paragraph 9 on page 6 of the Office Action are addressed in the new claims. Specifically, the new claims do not recite the phrase "a polynucleotide encoding a protein comprising the amino acid sequence of SEQ ID NO:2 in which one or more amino acids are replaced, deleted, inserted, and/or added." Instead, new claims 43-46, 47, 48-50, 51-53 and 56-58 are limited to polypeptides that are enone reductases that reduce the carbon-carbon double bond of an α,β-unsaturated ketone, using NADPH as an electron donor, to produce a corresponding saturated hydrocarbon. Claims 43-46 are further limited to a polypeptide that is at

least 80%, 85%, 90% or 95% percent identical to SEQ ID NO:2, respectively. Claim 47 is further limited to polypeptides encoded by a nucleic acid consisting of the complement of a nucleic acid that hybridizes under stringent conditions to a nucleic acid consisting of the nucleotide sequence of SEQ ID NO:1. Claims 48-50 are further limited to a polypeptide encoded by a nucleic acid that is at least 80% (or 90% or 95%) identical to SEQ ID NO:1. Claims 51-53 are further limited to a polypeptide comprising additional physical and functional characteristics of the claimed enone reductase. Finally, claims 56, 57 and 58 are further limited to an isolated polypeptide comprising SEQ ID NO:2 with 0 to 50, 0 to 30, and 0 to 10 conservative amino acid substitutions, respectively.

For those polypeptides not explicitly disclosed, but encompassed by the above-identified claims, Applicants submit that one of ordinary skill can produce, without undue experimentation, additional polypeptides that possess the enzymatic activities recited in the claims. The skilled artisan could easily manufacture additional enone reductases that are at least 80%, 85%, 90% or 95% identical to the polypeptide of SEQ ID NO:2 and test them to identify those with the recited activity. Applicants have taught how to assay for an enzyme that possesses the enone reductase activity in Examples 1-7 (also see page 8, lines 21-26 for a description of an exemplary enone reductase assay). Moreover, the specification provides the results of a BLAST search conducted to identify nucleic acid sequences encoding polypeptides having significant sequence homology to SEQ ID NO:2 (see page 14, lines 6-29). Three homologs, YNN4 (SEQ ID NO:4), YL60 (SEQ ID NO:6) and YCZ2 (SEQ ID NO:8), were identified as having 54%, 51% and 53% amino acid sequence identity to SEQ ID NO:2, respectively. These results clearly indicate that the specification, coupled with the knowledge of the skilled artisan, reasonably provide enablement for an enone reductase that is at least 80% identical SEQ ID NO:2.

Producing a polypeptide that comprises conservative amino acid substations is a trivial task that any molecular biologist could accomplish using standard recombinant DNA and polypeptide expression techniques. For example, the polypeptides claimed in claims 56-58 comprise an amino acid sequence that is, at most, 14% different from SEQ ID NO:2. Further, any amino acid that is substituted for a particular residue in SEQ ID NO:2 must represent a

"conservative" substitution. The skilled artisan will have little difficulty making such conservative substitutions and testing the resulting polypeptides for the recited enzymatic activity. One would expect to produce a reasonably high number of active enzymes in view of the use of conservative amino acid substitutions.

In another example, the skilled artisan could make a polypeptide comprising an amino acid sequence at least 80% identical to SEQ ID NO:2 by utilizing the algorithm described on page 13, lines 12-31, of the specification. Subsequently, the skilled artisan could determine, absent undue experimentation, whether or not the polypeptide possesses enone reductase activity. By providing the appropriate nucleic acid and amino acid sequences, information regarding identifying homologs of the nucleic acid and amino acid sequences described in the specification, and enzymatic assays for determining enone reductase activity, Applicants have presented the skilled artisan with all the information necessary to make the claimed compositions using only routine experimentation. Once made, the polypeptides can be used as described in the specification. There is no reason to believe that the quantity of experimentation required to practice this invention is excessive. For example, one need only to prepare variant polypeptides using routine and often automated procedures, determine whether the degree of homology of the encoding DNA is sufficient for it to hybridize to SEQ ID NO:1 under the recited conditions, and determine its enone reducatse characteristics using known assay methodologies or those described at page 12, lines 22-32, of the present specification. All methodologies for performing such tasks are routine and well known in the art and/or disclosed in the present specification and require no inventive effort or thought.

Finally, while claims 51-53 do not recite particular amino acid or nucleic acid sequences, the claims are limited to polypeptides that possess all of the physical and functional characteristics recited in the claim. The skilled artisan can easily identify the molecular weight, pH, and optimal temperature of a particular polypeptide. The specification teaches how to assay for the enone reductase activities that the polypeptide must possess. The specification further teaches how to assay for the particular substrate specificity recited in the claim.

In view of the above discussion, Applicants submit that the pending claims comply with the "enablement" requirement of 35 U.S.C. §112, first paragraph.

***Written Description***

Claims 1-3, 16 and 17 stand rejected under 35 USC §112, first paragraph, as allegedly containing subject matter which was not described in such a way as to reasonably convey to one skilled in the art that the inventors had possession of the full breadth of the claims. This rejection is moot in view of the cancellation of claims 1-3, 16 and 17. Applicants traverse this rejection as it may apply to the pending claims.

The standard for determining compliance with the written description requirement is "does the description clearly allow persons of ordinary skill in the art to recognize that he or she invented what is claimed." In re Gosteli, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989). The standard for determining sufficiency of the description is "factual and depends on the nature of the invention and the amount of knowledge imparted to those skilled in the art by the disclosure." In re Wertheim, 541 F.2d at 262 (citing In re Ruschig, 379 F.2d 990, 995-96 (C.C.P.A. 1967)).

Applicants submit that the pending claims simply do not allow for a substantial amount of variability in structure or function of the claimed polypeptides. In other words, one skilled in the art would not expect the genus of proteins encompassed by these claims to have substantial variation. For example, with regard to new claims 43-46, polypeptides that are highly homologous to SEQ ID NO: 2 are likely to possess the recited "enone reductase activity." Any such proteins would necessarily be significantly similar in terms of structure. Similar arguments are applicable to the polypeptides claimed in claims 47, 48-50 and 56-58. The new claims encompass a narrow range of variants including those (a) having up to 50 conservative amino acid substitutions, (b) encoded by the complement of a nucleic acid hybridizing under high stringency conditions with the nucleic acid of SEQ ID NO: 1, or (c) having at least 80% identity to the amino acid sequence of SEQ ID NO: 2. The genus is neither widely divergent nor highly variable. As there is little variation within the claimed genus, a single example is sufficient to

demonstrate possession of the claimed genus of polypeptides. This conclusion is consistent with USPTO policy regarding written description analysis set forth the Revised Interim Written Description Guidelines published January 5, 2001, particularly the Training Materials accompanying same. For example, in Training Materials Example 14, involving a claim analogous to some of the pending claims, the PTO concluded that since all the variants must possess the specific catalytic activity and must have a high degree of homology to the reference sequence, the genus of proteins that must be variants does not have substantial variation. Accordingly, a single disclosed species was representative of the genus. Moreover, the disclosure of the species would reasonably convey to one of ordinary skill in the art that the inventors had possession of the genus and that invention includes the genus.

Claims 51-53, as previously noted, do not recite a particular amino acid or nucleic acid sequence. However, claims 51-53 are limited to those polypeptides possessing specific functional and structural characteristics, such as enzymatic activity and molecular weight, which clearly indicate that the inventors were in possession of the claimed polypeptides at the time the application was filed.

In view of the above discussion, Applicants submit that the pending claims comply with the "written description" requirement of 35 U.S.C. §112, first paragraph.

## IV. Rejection under 35 U.S.C. §102(b)

Claim 16 stands rejected under 35 U.S.C. §102(b) as anticipated by each of Shimoda, Wanner and Kawai. This rejection is moot with regard to canceled claim 16. Applicants traverse the rejection as it may apply to the pending claims.

According to the Office Action, the cited references disclose enone reductases. Applicants submit that the limitations recited in new claims 43-58 clearly distinguish the claimed polypeptides from those described in the cited references. Accordingly, Applicants submit that the pending claims claim novel polypeptides not encompassed by any of the cited references.

In summary, for the reasons set forth herein, Applicants maintain that claims 43-58 clearly and patentably define the invention. Applicants respectfully request the allowance of the claims which are now pending. If the Examiner would like to discuss any of the issues raised in the Office Action, Applicants' representative can be reached at (617) 542-5070. Payment of the excess claim fees and the fees associated with the one-month extension, set forth in 37 CFR §1.17(a)(2), is submitted herewith. Please charge any additional fees, or make any credits, to Deposit Account No. 06-1050.

Respectfully submitted,

Date: 12/9/03

Reg No. 40,900

Janis K. Fraser, Ph.D., J.D. for
Reg. No. 34,819

Fish & Richardson P.C.
225 Franklin Street
Boston, MA 02110-02804
Telephone: (617) 542-5070
Facsimile: (617) 542-8906

10323598.1.doc